

REMARKS

Claims 2, 3, 5, 7, 8, 39-43, 45-57 and 59-68 are pending in the application. Claims 1, 4, 6, 9-38, 44 and 58 have been previously canceled. Applicants respectfully request reconsideration of the application in view of the remarks made herein. Accordingly, no new matter has been added.

Rejections under 35 U.S.C. § 112, first paragraph (Written Description)

The Examiner has rejected claims 2, 3, 5, 7, 8, 39-43, 45-57 and 59-68 under 35 U.S.C. § 112, first paragraph for allegedly lacking written description. This rejection is respectfully traversed.

In continuing to maintain the new matter rejection, the Examiner asserts on page 3 of the Final Office Action that "...the method of modulating the proliferation of a cell by contacting the cell with an agent that either modulates the expression or activity of a TRADE family polypeptide (as claimed in claim 15 and 16) does not require the cell to possess TRADE activity." In addition, the Examiner also states that "this limitation does not have support from the instant specification elsewhere either." (Office Action, page 3)

Applicants respectfully disagree. The Applicants maintain that the specification provides adequate written description support for such a disclosure. In particular, the Applicants note that the specification provides support for the subject method of modulating the proliferation of a cell by contacting the cell with an agent that either modulates the expression or activity of a TRADE family polypeptide in which the cell possesses TRADE activity at, for example, various tissues and organs that express human TRADE are provided on page 8, line 29 through page 9, line 5 and the term "Trade activity" is described on page 11, line 1-14.

The Applicants point out that the specification includes a section entitled "Methods of Modulating TRADE" on p. 19, line 18 through page 25, line 2. In particular, this section specifically states that "The modulatory methods of the invention involve contacting the cell with an agent that modulates TRADE expression and/or activity such that TRADE expression and/or activity in the cell is modulated." (P. 19, line 27-29).

Furthermore, as presented in the previous response, original claims 15, 16, 18-20 and 25 of the application recite as follows (emphasis added):

15. A method of modulating the proliferation of a cell comprising contacting the cell with an agent that modulates the expression of a TRADE family member polypeptide, wherein the cell is selected from the group consisting of an epithelial cell, a ductal epithelial cell, a carcinoma cell, and an adenocarcinoma cell, such that the proliferation of the cell is modulated.

16. A method of modulating the proliferation of a cell comprising contacting the cell with an agent that modulates the activity of a TRADE family member polypeptide, wherein the cell is selected from the group consisting of: an epithelial cell, a ductal epithelial cell, a carcinoma cell, and an adenocarcinoma cell such that the proliferation of the cell is modulated.

18. The method of claim 15 or 16, wherein the agent is a soluble form of a TRADE family polypeptide comprising a TRADE extracellular domain.

19. The method of claim 18, wherein the soluble form of a TRADE family polypeptide is a TRADE-Fc fusion protein.

20. The method of claim 15 or 16, wherein the agent consists essentially of a TRADE family extracellular domain.

25. The method of claim 16, wherein the activity is selected from the group of activities consisting of: ***activation of a JNK signaling pathway***, activation of an NFkB signaling pathway, and activation of apoptosis.

Based on the specification and the original filed claims, it would be clear to one of skill in the art that only cells with TRADE activity will respond to the administration of an extracellular portion of the TRADE polypeptide. The law is clear that, if a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if not every nuance of the claims is explicitly described in the specification, then the adequate written description requirement is met.¹

Therefore, the skilled artisan would fully understand that the subject methods for modulating TRADE activity in a cell with an agent that modulates TRADE expression and/or activity, specifically requires that the cell actually possess TRADE activity in order to be modulated. As such, the instant specification provides support for a method that includes modulating activation of an NFkB signaling pathway in a cell by contacting a cell having TRADE activity with a TRADE polypeptide as recited in the pending claims.

The written description requirement of 35 U.S.C. § 112, first paragraph, requires that the invention be described in such a way that those skilled in the art would recognize that the applicant had, as of the priority date of the application, possession of the invention. It is Applicants position that the written description requirement has been met. Accordingly, this rejection may be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph (Enablement)

The Examiner rejected claims 2, 3, 5, 7, 8, 39-43, 45-57 and 59-68 under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the enablement requirement. This rejection is respectfully traversed as applied and as it may be applied to the pending claims.

Independent claims 2 and 53, from which the remaining claims subject to the rejection depend, recite a method for modulating activation of an NFκB signaling pathway by contacting a cell having TRADE activity with a soluble form of a TRADE polypeptide comprising the extracellular domain of a TRADEα polypeptide.

According to the Office Action, the Examiner alleges that “the specification fails to demonstrate a soluble form of TRADE polypeptide that encoded by a polynucleotide 98% homologous to the polynucleotide encoding 1-168 amino acid of SEQ ID NO: 2 that functions as an antagonist of a TRADE ligand, and thereby modulates the NFκB activation in all cell types in vitro or in vivo.” (Office Action, p. 4)

As presented in the previous response, Applicants maintain that soluble forms of the TRADE polypeptide can be used as TRADE ligand antagonists.² Soluble TRADE peptides comprising the extracellular portion of the TRADE protein act as antagonists to TRADE ligand.³ This antagonism of TRADE ligand leads to change in the activity of the intracellular portion of the TRADE proteins expressed in a cell to which the soluble TRADE extracellular portion is administered to. As described in Example 4 of the instant application, modulation of the activity of the intracellular portion of the TRADE protein will lead to modulation of NFκB activity.

¹ *In re Alton* 76 F.3d 1168, 37 USPQ2d 1578 (Fed. Cir. 1996).

² See the instant specification at page 49, lines 15-19.

³ *Id.* from page 130, line 17 to page 131, line 6.

Applicants submit that the instant specification provides ample guidance which, when combined with the knowledge and skill in the art, provides an enabling disclosure for a method for modulating activation of an NFκB signaling pathway by contacting a cell having TRADE activity with a soluble form of a TRADE polypeptide comprising the extracellular domain of a TRADEα polypeptide as claimed.

Firstly, the specification discloses various different TRADEα polypeptides, e.g., Flag-TRADEα, Flag-TRADE 1-368, Flag-TRADE 1-328, Flag-TRADE 1-218 and Flag-TRADE 1-196, which modulate the activity of NFκB at p. 133, lines 8-24 and in Figure 9 and 14A. Accordingly, the specification has provided various examples of TRADEα polypeptides containing a TRADEα extracellular domain and having the ability to modulate NFκB signaling.

Secondly, the specification identifies certain TRADE domains and in particular, describes the extracellular domain comprising amino acid residues which correspond to residues 1-168 of SEQ ID NO: 2. In addition, Example 1 describes an exemplary protocol for molecular cloning and genetic mapping of TRADE and Figure 1 depicts the amino acid sequence comparison between the two human TRADE proteins of the invention (α and β).

Thirdly, Examples 2 and 3 demonstrate TRADEα and TRADEβ expression in various tissues and organs with the highest levels in adult prostate, lung, ovary, and fetal lung and liver. Further, immunohistochemistry demonstrated that TRADEα and TRADEβ are primarily localized in the prostate, parotid gland and testis to ductal epithelial tissues and that TRADE expression can be detected in adenocarcinomas.

Fourthly, TRADE activity is described in detail at p. 11, lines 1 through 14 and the NFκB signaling pathway is described at p. 11, line 23 through p. 12, line 2.

Additionally, the specification describes *in vitro* methods on p. 21, lines 4 through 9 and *in vivo* methods on p. 21, line 10 through p. 24, lines 30. TRADE fusion proteins are described on p. 47, line 25 through p. 50, lines 26 and TRADE agonists and antagonists are described at p. 50, lines 27 through p. 51, line 28.

Further, the specification describes isolated nucleic acid molecules encoding TRADE or portions thereof in great length, for example, from p. 27, line 24 through p. 43, line 16. Isolated TRADE proteins, fragments thereof and anti-TRADE antibodies are described at p. 43, line 19 through p. 66, line 28.

Moreover, recombinant expression vectors and host cells for expressing TRADE proteins or protein fragments in prokaryotic or eukaryotic cells is described at p. 67, line 1 through p. 76, line 15.

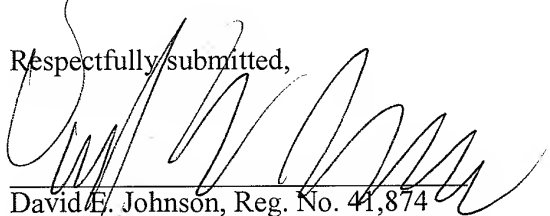
The instant specification also provides methods for identifying other TRADE modulating agents at p. 76, line 18 through p. 98, line 2.

Based on the above, the Applicants submit that the specification clearly enables one of skill in the art to practice the subject invention. In other words, Applicants submit that the instant specification provides ample guidance which, when combined with the knowledge and skill in the art, provides an enabling disclosure for a method for modulating activation of an NF κ B signaling pathway by contacting a cell having TRADE activity with a soluble form of a TRADE polypeptide comprising the extracellular domain of a TRADE α polypeptide as claimed.

CONCLUSION

The Applicants respectfully submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned below. The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-0580, Reference No. 22058-569.

Respectfully submitted,



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